

What is claimed is:

1. An isolated polypeptide, comprising an amino acid sequence selected from SEQ ID NO: 10 or 16.
2. The isolated polypeptide of claim 1,  
5 comprising SEQ ID NO: 10.
3. The isolated polypeptide of claim 1, comprising SEQ ID NO: 16.
4. An isolated polypeptide, comprising
  - a) an amino acid sequence having at least  
10 50% amino acid identity with SEQ ID NO: 18, and
  - b) an amino acid sequence selected from SEQ ID NOS: 8, 10, 12, 14, and 16, or a conservative variant thereof.
5. An isolated polypeptide, comprising an  
15 amino acid sequence selected from SEQ ID NOS: 2, 4 and 6, or a conservative variant thereof.
6. The isolated polypeptide of claim 5, wherein said polypeptide comprises an amino acid sequence  
20 selected from SEQ ID NOS: 2, 4 and 6.
7. The isolated polypeptide of claim 6, wherein said polypeptide consists of an amino acid sequence selected from SEQ ID NOS: 2, 4 and 6.
8. An EP<sub>4</sub> receptor variant binding agent, which  
25 binds SEQ ID NO: 10, or an epitope thereof.

9. The binding agent of claim 5, wherein said binding agent is an antibody, or antigen binding fragment thereof.

10. A cell, comprising the exogenously  
5 expressed polypeptide of claim 1, 4, or 5.

11. A method for identifying a compound that modulates an EP<sub>4</sub> receptor variant, comprising:

a) contacting said EP<sub>4</sub> receptor variant with a compound, wherein said EP<sub>4</sub> receptor variant is an  
10 isolated EP<sub>4</sub> receptor variant or an EP<sub>4</sub> receptor variant over-expressed in a genetically engineered cell, and

b) determining the level of an indicator, which correlates with modulation of said EP<sub>4</sub> receptor variant, wherein an alteration in the level of said  
15 indicator as compared to a control level indicates that said compound is a compound that modulates said EP<sub>4</sub> receptor variant.

12. The method of claim 11, wherein said alteration is an increase in the level of said indicator.

20 13. The method of claim 11, wherein said alteration is a decrease in the level of said indicator.

14. The method of claim 11, wherein said EP<sub>4</sub> receptor variant is a polypeptide comprising

a) an amino acid sequence having at least 50% amino acid identity with SEQ ID NO: 18, and

5                   b) an amino acid sequence selected from SEQ ID NOS: 8, 10, 12, 14, and 16, or a conservative variant thereof.

15                   15. The method of claim 11, wherein said EP<sub>4</sub> receptor variant is a polypeptide comprising an amino  
10 acid sequence selected from SEQ ID NOS: 2, 4 and 6, or a conservative variant thereof.

16. The method of claim 11, wherein said EP<sub>4</sub> receptor variant is an isolated EP<sub>4</sub> receptor variant polypeptide.

15                   17. The method of claim 11, wherein said EP<sub>4</sub> receptor variant is an EP<sub>4</sub> receptor variant over-expressed in a genetically engineered cell.

18. The method of claim 17, wherein said EP<sub>4</sub> receptor variant is exogenously expressed.

20                   19. The method of claim 11, wherein said indicator is calcium.

20. The method of claim 11, wherein said compound is a polypeptide.

25                   21. The method of claim 11, wherein said compound is a small molecule.

22. A method for identifying a compound that specifically binds to an EP<sub>4</sub> receptor variant, comprising:

a) contacting said EP<sub>4</sub> receptor variant with a compound, wherein said EP<sub>4</sub> receptor variant is an isolated EP<sub>4</sub> receptor variant or an EP<sub>4</sub> receptor variant over-expressed in a genetically engineered cell, and

b) determining specific binding of said compound to said EP<sub>4</sub> receptor variant.

23. The method of claim 22, wherein said EP<sub>4</sub> receptor variant is a polypeptide comprising

a) an amino acid sequence having at least 50% amino acid identity with SEQ ID NO: 18, and

b) an amino acid sequence selected from SEQ ID NOS: 8, 10, 12, 14, and 16, or a conservative variant thereof.

24. The method of claim 22, wherein said EP<sub>4</sub> receptor variant is a polypeptide comprising an amino acid sequence selected from SEQ ID NOS: 2, 4 and 6, or a conservative variant thereof.

25. The method of claim 22, wherein said EP<sub>4</sub> receptor variant is an isolated EP<sub>4</sub> receptor polypeptide.

26. The method of claim 22, wherein said EP<sub>4</sub> receptor is an EP<sub>4</sub> receptor variant over-expressed in a genetically engineered cell.

27. The method of claim 26, wherein said EP<sub>4</sub> receptor variant is exogenously expressed.

28. The method of claim 22, wherein said contacting occurs *in vitro*.

29. The method of claim 22, wherein said compound is a polypeptide.

5           30. The method of claim 22, wherein said compound is a small molecule.

31. A method for identifying a compound that differentially modulates an EP<sub>4</sub> receptor variant, comprising:

- 5 a) contacting said EP<sub>4</sub> receptor variant with a compound, wherein said EP<sub>4</sub> receptor variant is an isolated EP<sub>4</sub> receptor variant or an EP<sub>4</sub> receptor variant over-expressed in a genetically engineered cell;
- b) determining the level of an indicator which correlates with modulation of said EP<sub>4</sub> receptor  
10 variant;
- c) contacting a second receptor with said compound;
- d) determining the level of a corresponding indicator which correlates with modulation  
15 of said second receptor; and
- e) comparing the level of the indicator from step (b) with the level of the corresponding indicator from step (d), wherein a different level of the indicator from step (b) compared to the level of the  
20 corresponding indicator from step (d) indicates that said compound is a compound that differentially modulates said EP<sub>4</sub> receptor variant.

32. The method of claim 31, wherein said second receptor is a different EP<sub>4</sub> receptor variant.

25 33. The method of claim 31, wherein said second receptor comprises the amino acid sequence SEQ ID NO: 18, or a functional fragment thereof.

34. The method of claim 31, wherein the level of said indicator from step (b) is greater than the level of said corresponding indicator from step (d).

35. The method of claim 31, wherein the level  
5 of said indicator from step (b) is less than the level of said corresponding indicator from step (d).

36. The method of claim 31, wherein said EP<sub>4</sub> receptor variant is a polypeptide comprising

10 a) an amino acid sequence having at least 50% amino acid identity with SEQ ID NO: 18, and

b) an amino acid sequence selected from SEQ ID NOS: 8, 10, 12, 14, and 16, or a conservative variant thereof.

15 37. The method of claim 31, wherein said EP<sub>4</sub> receptor variant is a polypeptide comprising an amino acid sequence selected from SEQ ID NOS: 2, 4 and 6, or a conservative variant thereof.

20 38. The method of claim 31, wherein said EP<sub>4</sub> receptor variant is an isolated EP<sub>4</sub> receptor polypeptide.

39. The method of claim 31, wherein said EP<sub>4</sub> receptor variant is an EP<sub>4</sub> receptor variant over-expressed in a genetically engineered cell.

25 40. The method of claim 39, wherein said EP<sub>4</sub> receptor variant is exogenously expressed.

41. The method of claim 31, wherein said indicator in step (b) is calcium.

42. The method of claim 31, wherein said compound is a polypeptide.

43. The method of claim 31, wherein said compound is a small molecule.

5           44. A method for identifying a compound that differentially binds to an EP<sub>4</sub> receptor variant, comprising:

          a) contacting said EP<sub>4</sub> receptor variant with a compound, wherein said EP<sub>4</sub> receptor variant is an  
10 isolated EP<sub>4</sub> receptor or an EP<sub>4</sub> receptor variant over-expressed in a genetically engineered cell;

          b) determining specific binding of said compound to said EP<sub>4</sub> receptor variant;

          c) contacting a second receptor with said  
15 compound;

          d) determining specific binding of said compound to said second receptor; and

          e) comparing the level of specific binding from step (b) with the level of specific binding from  
20 step (d), wherein a different level of specific binding from step (b) compared to the level of specific binding from step (d) indicates that said compound is a compound that differentially binds to said EP<sub>4</sub> receptor variant.

          45. The method of claim 44, wherein said  
25 second receptor is a different EP<sub>4</sub> receptor variant.



46. The method of claim 44, wherein said second receptor comprises the amino acid sequence SEQ ID NO: 18, or a functional fragment thereof.

47. The method of claim 44, wherein said  
5 different level of specific binding is an increased level of binding.

48. The method of claim 44, wherein said different level of specific binding is a decreased level of binding.

10 49. The method of claim 44, wherein said EP<sub>4</sub> receptor variant is a polypeptide comprising

a) an amino acid sequence having at least 50% amino acid identity with SEQ ID NO: 18, and

b) an amino acid sequence selected from  
15 SEQ ID NOS: 8, 10, 12, 14, and 16, or a conservative variant thereof.

50. The method of claim 44, wherein said EP<sub>4</sub> receptor variant is a polypeptide comprising an amino acid sequence selected from SEQ ID NOS: 2, 4 and 6, or a  
20 conservative variant thereof.

51. The method of claim 44, wherein said EP<sub>4</sub> receptor variant is an isolated EP<sub>4</sub> receptor polypeptide.

52. The method of claim 44, wherein said EP<sub>4</sub> receptor variant is an EP<sub>4</sub> receptor variant over-expressed  
25 in a genetically engineered cell.

53. The method of claim 52, wherein said EP<sub>4</sub> receptor variant is exogenously expressed.

54. The method of claim 44, wherein said contacting occurs *in vitro*.

5 55. The method of claim 44, wherein said compound is a polypeptide.

56. The method of claim 44, wherein said compound is a small molecule.

57. An isolated nucleic acid molecule,  
10 comprising a nucleotide sequence that encodes a polypeptide comprising

a) an amino acid sequence having at least 50% amino acid identity with SEQ ID NO: 18, and

b) an amino acid sequence selected from  
15 SEQ ID NOS: 8, 10, 12, 14, and 16, or a conservative variant thereof.

58. An isolated nucleic acid molecule,  
comprising a nucleotide sequence that encodes an amino acid sequence selected from SEQ ID NOS: 2, 4 and 6, or a  
20 conservative variant thereof.

59. The isolated nucleic acid molecule of claim 55, wherein said isolated nucleic acid comprises a nucleotide sequence that encodes an amino acid sequence selected from SEQ ID NOS: 2, 4 and 6.

60. The isolated nucleic acid molecule of claim 59, wherein said isolated nucleic acid consists of a nucleotide sequence that encodes an amino acid sequence selected from SEQ ID NOS: 2, 4 and 6.

5           61. The isolated nucleic acid molecule of claim 58, wherein said nucleotide sequence is selected from SEQ ID NOS: 1, 3, and 5.

62. A vector, comprising the isolated nucleic acid molecule of claim 57 or 58.

10           63. A host cell, comprising the vector of claim 62.